Clinical Medicine 2011, Vol 11, No 3: 275–8

Sleep apnoea syndromes and the cardiovascular system

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The sleep apnoea syndromes (SAS) comprise three main disorders:

- obstructive sleep apnoea (OSA)
- central sleep apnoea (CSA)
- Cheyne-Stokes respiration (CSR).

CSA and CSR occur mainly in patients with established cardiovascular disease, while the main risk for OSA is obesity. OSA patients often have high cardiovascular risk – smoking, type 2 diabetes, hypertension and lipid abnormalities being common. Indeed, the obesity pattern associated with OSA (truncal obesity) is itself associated with higher cardiovascular risk.

As the prevalence of obesity increases so does OSA; thus, historical data for prevalence of OSA (2–4% for adult males)[1] are likely to be an underestimate. For an average 0.5 million population, current estimates suggest at least 500 new referrals for OSA are likely per year with 200 new patients needing treatment with continuous positive airway pressure (CPAP).[2]

Early epidemiological studies were confounded by the strong associations between OSA and established cardiovascular risk markers, making it difficult to demonstrate an independent contribution from sleep apnoea. There is now a large volume of work linking sleep apnoea and cardiovascular disease. This link is important: since sleep apnoea is so prevalent, it may contribute to the enormous burden of cardiovascular morbidity and mortality.

OSA causes sleepiness, which reduces quality of life, and is also associated with a sixfold rise in risk of road traffic accident. CPAP is an established cost-effective treatment which improves sleepiness and quality of life in people with moderate to severe OSA.[3] If CPAP treatment improves cardiovascular outcome in addition to current primary and secondary prevention measures, this should prompt a more active screening process for sleep apnoea in patients with cardiovascular disease.

Pathophysiology

It has been hypothesised that snoring vibrations might damage carotid vessel walls inducing plaque formation.[4] Perhaps 30–40% of snorers have occasional OSA where the pharynx collapses during inspiration, obstructing airflow. Respiratory effort continues, generating large negative intrathoracic pressure swings. This raises left ventricular (LV) transmural pressure and afterload, increasing cardiac work at a time when the apnoea causes hypoxia, hypercapnia and sympathetic activation. After a variable time the patient arouses, reopens the airway and breathing resumes. At arousal, sympathetic activation raises heart rate and blood pressure (BP) sometimes by as much as 60 mmHg.[5] The intrathoracic pressure swings are less in CSA because the apnoeas occur through altered respiratory drive. However, the same powerful physiological stressors are present which can adversely affect cardiac function.

It is easy to see how the hypoxia, hypercapnia and sympathetic activation occurring at a time of peak myocardial oxygen demand might adversely affect the heart, promoting regional ischaemia, arrhythmias or plaque destabilisation. There are wider consequences throughout the vascular tree, with OSA increasing systemic inflammation,[6] triggering endothelial and circulating cells to release inflammatory cytokines,[7] adhesion molecules and growth promoters. Sympathetic activation alters lipid and glucose metabolism, increasing free radical production and endothelial injury, vasoconstriction vessel remodelling, increasing vessel wall stiffness and platelet aggregation. These processes may promote a vicious circle of deteriorating endothelial, small and large vessel function including the heart and great vessels. Many of these inflammatory pathways have shown improvements with CPAP treatment.[7]

Hypertension

A number of epidemiological longitudinal studies have confirmed an independent relationship between OSA and both the prevalence and incidence of hypertension.[8,9] Increasing severity of sleep apnoea is associated with increased likelihood of hypertension. OSA increases BP variability, raises BP during the night and daytime, is associated with a lack of nocturnal dip in BP and is often found in drug-resistant hypertension. CPAP treatment reduces BP by about 2–5 mmHg.[10] CPAP, may be more effective in reducing BP in those with severe disease with sleepiness, and improved CPAP compliance potentially predicts a better response.[11]

Coronary arterial disease

OSA is linked to increased coronary artery calcification, prevalence of myocardial infarctions and incidence of coronary artery disease (CAD) and cardiovascular mortality.[12,13] In CAD, OSA is associated with worse outcomes following primary and elective angioplasty:[14]

- reduced recovery of myocardium and ejection fraction
- increased risk of re-stenosis
- the need for coronary bypass grafting
- death.

Better outcomes are associated with CPAP treatment. If it is tolerated, CPAP is linked to reduced nocturnal angina, episodes of ST segment depression, future acute coronary syndromes, revascularisation procedures, admissions and cardiovascular deaths.[15]

Despite the strong circumstantial evidence, as yet there is no published, large, randomised controlled trial concerning reduced cardiovascular risk with the use of CPAP although several are underway.

Arrhythmias

A number of arrhythmias occur in SAS incidentally or in response to cardiac interventions. Heart rate varies through each individual cycle of apnoea. Heart rate variability is increased in SAS and can be used to screen for SAS. As arousal terminates an apnoea, resumption of ventilation leads to a tachycardia via sympathetic activation and changes in venous return. The attendant BP surge causes baroreflex-mediated bradycardia via the vagus nerve, with significant cardiac pauses reported frequently in patients with otherwise normal sino-atrial node activity.

Atrial fibrillation (AF) is very common in heart failure with Cheyne-Stokes breathing, and can also be triggered by OSA.[16] Ventricular tachycardia and complex ventricular ectopy are described, mainly in OSA, with arrhythmia frequency increasing with worse hypoxaemia. CSR can trigger malignant arrhythmias, and is also associated with increased frequency of appropriate shock delivery in patients with severe cardiac failure and implanted defibrillators. Studies of patients with long-term ECG monitoring confirm that the arrhythmias are triggered by apnoeic events. CPAP treatment reduces both arrhythmia frequency overall and recurrence of AF following DC cardioversion.[17]

Heart failure

Sixty per cent of people with heart failure will have OSA, CSA or CSR. Conversely, LV impairment, particularly diastolic dysfunction, is common in people with OSA. Notably, even children naïve to standard cardiovascular risks demonstrate ventricular hypertrophy in association with OSA.[18]

In patients with confirmed heart failure, SAS is commoner in men. CSR is associated with increased age, AF, severe heart failure, raised pulmonary capillary wedge pressure and low daytime $PaC0_2$.[19] OSA is associated with increased body mass index. Both OSA and CSA/CSR may occur in the same patient through a single night. On lying recumbent, peripheral oedema shifts centrally. In the lungs this alters capillary wedge pressure and respiratory drive, and in the upper airway, oedema may promote obstruction.

OSA is associated with incident heart failure in men.[12] Prognosis is worse in heart failure patients with SAS, possibly through increased sympathetic activity. Control of LV function with cardiac resynchronisation therapy or heart transplantation can cure central sleep apnoea and is associated with improved prognosis. CPAP in patients with heart failure and OSA can improve quality of life, reduce arrhythmias and improve ejection fraction.[20] A large randomised controlled trial of CPAP in patients with heart failure and CSA demonstrated no benefit in mortality overall, but there was some suggestion that mortality improved in patients in whom CSA was controlled.[21] Trials of more complex ventilators are underway looking at mortality end-points in heart failure with sleep apnoea.

In the acute setting, patients may present with decompensated LV failure with pulmonary oedema. Alongside the standard cardiac treatments, CPAP and non-invasive ventilation (NIV/BILEVEL) can be used if initial treatment with high-flow oxygen via re-breathe mask fails to improve hypoxaemia.[22] CPAP set at 10 cm water pressure should be delivered with supplemental oxygen to increase alveolar partial pressure of oxygen, improve recruitment of alveoli, offload respiratory muscles and help to clear lung water. NIV can be used for patients in type 2 respiratory failure. In this situation NIV is best delivered by oxygen-driven devices in a high dependency setting where blood gas monitoring, close supervision and ventilator adjustment are possible.

Alternatively, patients may be admitted in the acute setting with cor pulmonale

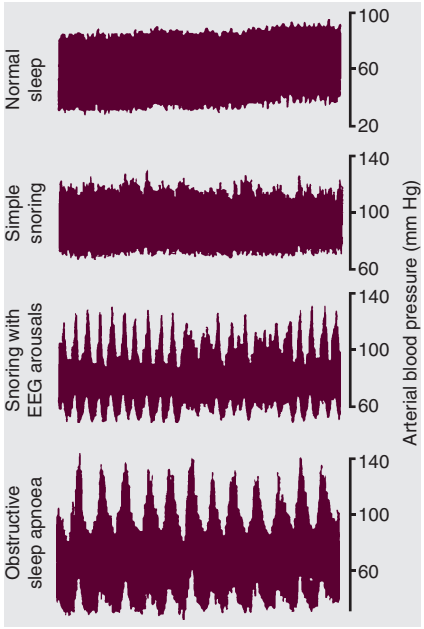

Fig 1. Blood pressure swings measured by Finapres non invasive finger plethysmography during sleep. Showing a progressive increase in blood pressure variability through snoring to obstructive sleep apnoea.

Key points

- Obstructive sleep apnoea (OSA) is very common in patients with cardiovascular disease (CVD) and is associated with a worse prognosis
- Patients with CVD should be screened for sleep apnoea
- CVD risk should be measured and addressed in all patients with OSA
- Compliance with continuous positive airway pressure treatment may reduce cardiovascular morbidity
- Substantial weight loss can cure sleep apnoea and reduce cardiovascular risk

KEY WORDS: cardiovascular risk, central sleep apnoea, Cheyne-Stokes breathing, continuous positive airway pressure, obstructive sleep apnoea

and generalised oedema secondary to a combination of chronic hypoventilation, obesity and coexistent lung disease, cardiac and renal disease. Decompensation may be gradual or precipitated by sedative use or concurrent infection. In this setting, NIV can be used over several days, in combination with standard treatments, to improve blood gases and ventilatory drive and help offload the oedema.

Stroke

OSA is a risk factor for stroke.[23] SAS are common after stroke, occurring in equal measure with haemorrhagic and thrombotic stroke and in any territory. They can be obstructive, central or mixed. Sleep apnoea conveys a poor prognosis after stroke; this can be improved by CPAP, although facial droop and poor compliance may limit its use. In the longer term, CPAP can reduce the incidence of further cardiovascular events in stroke patients.[24]

Death

Sleep apnoea increases mortality independent of the common confounders for risk of cardiovascular disease. In observational studies CPAP, if tolerated, improves overall mortality and cardiovascular disease-related mortality, returning risk to that of a normal population[13] — although as yet no large prospective trials of CPAP have confirmed this. Since CPAP is so effective in controlling symptoms of daytime sleepiness, no such trial is likely to be performed in symptomatic patients. A number of studies are ongoing or due to report on whether CPAP might reduce risk in asymptomatic subjects.

Summary

Management of SAS and cardiovascular disease risk should be closely linked. It is important to screen for cardiovascular disease risk in patients with SAS and vice versa. CSA/CSR may be improved by ventilation strategies in heart failure, but benefit remains to be proven. For OSA, although CPAP may reduce cardiovascular disease risk, its main benefit is symptom control. In the longer term, CPAP should be used alongside standard cardiovascular risk reduction strategies including robust weight management programmes, with referral for bariatric surgery in appropriate cases. CPAP and NIV should be considered for acute admissions with decompensated cardiac failure.

Conflict of interest

JCP is involved in research in the field of sleep medicine, including a commercially funded study of adaptive servo-ventilation in central sleep apnoea with heart failure, sponsored by ResMed. He has received sponsorship to attend and lecture at scientific meetings from Astra Zeneca, Glaxo Smith Kline and Resmed.

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Insomnia: evidence-based approaches to assessment and management

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Sleep disturbances are the most commonly reported psychological symptoms in Britain.[1] Prevalence estimates of chronic symptoms accompanied by daytime consequences range from 8–12% of the adult population.[2] Age-specific rates, however, show a steady rise in prevalence across the lifespan, from 3–5% at age 18–25 to 25–30% age 65 and over.[2] At all ages, women generally report higher (though sometimes only marginally) rates of insomnia than men. Insomnia risk is also greatly elevated among those with long-term health conditions. Analyses controlling for age and gender, for example, indicate that heart disease, memory problems, depression and pain are all independently associated with an 80–150% increased odds of insomnia symptoms.[3] Caring environments also jeopardise sleep quality. Insomnia risk is significantly increased among those providing care at home for a dependent relative or spouse.[4] Hospitals (through, for example, noise, unfamiliarity, patient anxiety, association with acute illness episodes, side effects of treatment regimens) remain a robust and complex cause of inpatient sleep disturbances.[5]

Incidence data are scarce but the General Practice Research Database suggests an incidence of all sleep disorder diagnoses of 12.5/1,000 patient years.[6] Excluding non-insomnia sleep disorders (eg obstructive sleep apnoea, restless legs syndrome, narcolepsy), insomnia diagnoses probably account for at least half of these cases.

Diagnosis

Insomnia is characterised by a complaint of difficulty initiating or maintaining sleep, or of non-restorative sleep despite adequate opportunities to sleep.[7,8] For a diagnosis of insomnia these difficulties should occur three or more times a week, persist for at least a month and be associated with impaired social and/or occupational functioning. Most people with insomnia report symptoms of daytime fatigue, but few (about 20–25%) report symptoms of daytime sleepiness (ie increased daytime sleep tendency). Other daytime symptoms can include mood disturbances, impaired concentration and, within the working population, degraded occupational performance.

Given this emphasis on symptom duration (⩾4 weeks), most insomnias can be considered chronic. Sleep disturbances arising from episodic homeostatic (as in occupational sleep loss) or circadian (as in jet-lag) challenges should be given time to self-correct before treatments are initiated. However, short-term sleep disturbances which can arise in the context of hospitalisation may, in the patient's interest, be considered for immediate (and short-term) treatment.[9]

What causes insomnia?

Research evidence supports the view that chronic insomnia results from the interaction of three separate factors:

1 *predisposing*: inherent psychological vulnerability characterised by higher levels of trait anxiety, a susceptibility to cognitive intrusions and attentional bias
2 *precipitating*: sleep-disturbing physical, psychological or situational events
3 *perpetuating*: maladaptive behavioural responses to sleep disturbance which, over time, help to maintain insomnia as a chronic problem.

This interactive model helps to explain why some precipitating events (eg occupational stress, childbirth, bereavement, illness) can disturb sleep in most people